Table 2
Differences in dGEMRIC indices* at each subregion and each time point. * Values in milliseconds. ** Statistically significant defined as p <0,05. *** Trend. cMF = central medial femur; MT = medial tibial plateau; pMF = posterior medial femur; SE - standard error. BL = baseline; 6M = 6 months follow-up; IY= 1 year follow-up.

Region		Model (1)		Model (2)			
		β(SE)	P**	β(SE)	P**		
cMF	(BL) OA vs. no-OA	**-92.99 (19.35)**	**<.0001**	2.61 (25.42)	1.00		
	(6M) OA vs. no-OA	**-97.48(17.83)**	**<.0001**	-9 38 (23.46)	0.99		
	(IY) OA vs no-OA	**-101.53(19.74)**	**<.0001**	-4 26 (25.83)	1.00		
MT	(BL) OA vs, no-OA	**-76.58 (16.27)**	**<.0001**	-12.75(24 62)	0.99		
	(6M) OA vs. no-OA	**-94.04 (18.00)**	**<.0001**	-31.37(5,70)	0.82		
	(1Y)OA vs no-OA	**-63,60 (17.47)**	**0.001**	1.30 (25.96)	1.00		
pMF	(BL) OA vs no-OA	-54.50 (21.63)	0.12	19.71(31.51)	0.98		
	(6M) OA vs. no-OA	**-64.96(20,17)**	**0.02**	2.85 (30.55)	1.00		
	(1Y) OA vs. no-OA	-41.52(19.79)	0.29	37.56(30.46)	0.81		
cMF	BL	KL Grade	1 vs. 0	-36.60 (57.14)	1.00	-5.93 (52.01)	1.00
			2 vs. 0	-56.13(23.65)	0.43	21.13 (27.79)	0.99
			3 vs. 0	**-138.91 (24.96)**	**<.0001**	-34.93 (31.59)	0.99
	6M	KL Grade	1 vs. 0	-30.29 02.70)	1.00	-5.32 (43.79)	1.00
			2 vs. 0	-70.43(21.95)	0.07***	4.05 (25.16)	1.00
			1 vs. 0	**-131.47 (23.40)**	**<0001**	-30.24 (29.15)	0.99
	1Y	KL Grade	1 vs. 0	-79.97(57.56)	0.96	-43.00 (52.93)	0.99
			2 vs. 0	-63 43 (23.93)	0.26	20.44 (28.10)	0.99
			3 vs. 0	**-153.08 (25.26)**	**<0001**	-54.30 (31 92)	0.86
MT	BL	KL Grade	1 vs. 0	-30.35(48.47)	1.00	-12.67 (47.83)	1.00
			2 vs. 0	-51 76(20.06)	0.30	-2.46(26.57)	1.00
			3 vs. 0	**-108.02 (21.18)**	**<0001**	-42.86 (30.37)	0.95
	6M	KL Grade	1 vs. 0	-22.57(53.35)	1.00	0.52(51.29)	1.00
			2 vs. 0	-70.97 (22.26)	007***	-15.21 (27.92)	1.00
			3 vs. 0	**-122.70 (23.78)**	**<0001**	-67.75 (32.07)	0.61
	IV	KL Grade	1 vs. 0	0.60 (51.32)	1.00	19.12(51.94)	1.00
			2 vs. 0	-24.08 (21.22)	0.99	26.93 (27.97)	0.99
			3 vs. 0	**-109.15 (22-41)**	**0.001**	-(4.14 (31.83)	0.96
pMF	BL	KL Grade	1 vs. 0	56.43 (64.61)	0.99	86.04 (61.07)	0.95
			2 vs. 0	-21.44(26.73)	0.99	52.10(33.63)	0.92
			3 vs. 0	-87.38 (23.22)	0.09***	-4.76(33.40)	1.00
	6M	KL Grade	1 vs. 0	137.04 (59 44)	0.47	163.93 (56.15)	0.11
			2vs. 0	45.36(24.73)	0.79	20.18 (32.11)	1.00
			3 vs. 0	-74.29 (26.32)	0.18	8.78(37.03)	1.00
	1Y	KL Grade	1 vs. 0	62.15 (59.56)	0.99	97.79 (57.29)	0.66
			2 vs. 0	-20.47(24.63)	0.99	60.70(32.37)	0.77
			3 vs. 0	-59.99(26.00)	0.47	26.26(37.10)	0.99

Conclusion: In this sample of middle-aged women, the cartilage matrix composition status as assessed by dGEMRIC had significant relationships with OA knees and knees with KL grade 3. However, after adjustments for factors known to be associated with cartilage degeneration, no significant relationships were demonstrated.

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THE MRI DEFINITION OF KNEE OSTEOARTHRITIS: COMPARISON WITH RADIOGRAPHY AND ASSOCIATION WITH KNEE PAIN IN MIDDLE-AGED WOMEN

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Purpose: A magnetic resonance imaging (MRI) definition of (OA) was proposed in 2011 by Hunter et al.. In order to find out if this MRI definition detects OA in an earlier stage than the Kellgren and Lawrence criteria (K&L) on radiography, the definition needs further testing especially in persons with early signs of knee OA. The goal of the present study is therefore to determine the relationship between the MRI definitions of patellofemoral OA (PF OA) and tibiofemoral OA (TF OA) compared with the K&L score for knee OA. Furthermore, we test the association between the MRI definitions and knee pain at baseline, persistent knee pain after two years of follow-up and new knee pain after two years of follow-up.
Methods: 891 females of an open population-based cohort (45-60 years at baseline) had radiography and MRI of their knees at baseline. All radiographs were scored with the K&L criteria. All MRIs were assessed with a comprehensive semiquantitative scoring system. To diagnose knee OA we used the MRI definition proposed by Hunter et al.. At baseline and after 2 years all women filled in knee specific questionnaires. Pain at baseline was defined as current knee pain and pain in the past year. Pain at follow-up was defined as current knee pain, pain in the past year, persistent knee pain and new knee pain. Percentage agreement between the MRI definitions and the K&L criteria were calculated, as well as sensitivity and specificity with K&L≥2 as reference standard. With multivariate GEE analysis the associations between the MRI definition and the different knee pain definitions were assessed, as well as the association between the K&L criteria and the different knee pain definitions. All associations were adjusted for age and body mass index (BMI).
Results: Mean age of the women was 55.0 years; mean BMI of the population was 27.0kg/m2. Twice as many knee OA cases were defined with the MRI definition of TF OA (9.1%) than with the radiological definition (K&L≥2: 4.4%). Almost 8% of the knees were classified as MRI based PF OA, and 13.7% of the knees met MRI criteria for PF and/or TF OA. One-hundred-fifteen knees were classified with MRI TF OA, while these knees only showed K&L<2 and there did not meet radiographical OA criteria . Thirty-three knees were classified with K&L≥2 and not diagnosed with MRI TF OA. The agreement between the MRI definitions and K&L≥2 was highest for MRI TF OA (91.5%); sensitivity (55.8%) and specificity (93.1%) were moderate to good (Table 1). Associations between knee pain at baseline and MRI TF OA (OR ranged from 3.21-4.98), TF and/or PF OA (OR ranged from 2.59-4.17), and K&L≥2 (OR ranged from 4.22-6.03) were statistically significant (p<0.001). The association between PF OA and knee pain at baseline was only statistically significant for current knee pain. The predictive association between persistent knee pain and the definitions of knee OA were all significant (OR ranged from 3.14-5.30, p<0.001), except for the cut-off K&L≥1 at two years follow-up.

Table1
Agreement, sensitivity and specificity between the MRI definitions and K&L

	K&L≥1			K&L≥2		
	Agreement (%)	Sensitivity (%)	Specificity (%)	Agreement (%)	Sensitivity (%)	Specificity (%)
MRI TF OA	81.0	24.0	94.5	91.6	55.8	93.1
MRI PF OA	79.2	15.9	94.3	89.9	22.4	93.0
MRI TF and/or PF OA	79.3	31.5	90.6	87.3	59.7	88.5

K&L: Kellgren and Lawrence classification system; MRI: Magnetic resonance Imaging; PF OA: patellofemoral osteoarthritis; TF OA: tibiofemoral osteoarthritis. K&L is reference standard.

No significant associations were found for prediction of new knee pain after 2 years.

Conclusions: In this early OA population, the agreement of the MRI definition for knee OA and the reference standard K&L criteria is good. Compared to the K&L criteria there were twice as many cases 'diagnosed' with knee OA using the MRI definition (TF OA). The association of the MRI definition and knee pain is similar to the association between the K&L criteria and knee pain. The lack of association between PF OA and most knee pain definitions might be due to a lack of other features, such as bone marrow lesion, in the MRI definition. None of the definitions predicts new knee pain at 2 years follow-up.

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BONE MARROW LESION REGRESSION IS ASSOCIATED WITH WORSENING PERI-ARTICULAR BONE: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: Reducing bone marrow lesion (BML) size (BML regression) may represent an important therapeutic goal for modifying osteoarthritis (OA) progression. However, the relationship between the progression and regression of BMLs and knee OA progression remains poorly understood. We evaluated the associations between BML volume change and changes in peri-articular bone mineral density (paBMD), a measure of bone quality, as well as radiographic scoring of subchondral sclerosis to better understand the role of bone remodeling in these relationships.

Methods: The sample comprised 404 participants in the Osteoarthritis Initiative (OAI) with weight-bearing posterior-anterior knee radiographs and magnetic resonance images (MRI) at the 24- and 48-month visits as well as dual-energy x-ray absorptiometry (DXA) at the 30-/36-month and 48-month visits. The right knee was assessed unless contraindicated. We used knee DXA scans to derive medial tibia (MT) paBMD and a paBMD ratio (MT paBMD divided by lateral tibia (LT) paBMD [M:L paBMD]; ICC > 0.99). Knee radiographs were scored for sclerosis (grades 0 to 3) in the MT (test-retest kappa = 0.76). Two raters determined BML volume on sagittal fat-suppressed MRI using a semi-automated segmentation method (ICC = 0.59 - 0.93). BML volume was calculated for the MT and LT. We excluded knees with LT BML volumes $\geq 0.50\ cm^3$ (at 24- or 48-month OAI visits) because we wanted to ensure that the LT was a good reference region for the M:L paBMD ratio, particularly since we were interested in changes in the MT. The cut point for LT BMLs was based on preliminary univariate analyses that suggested moderate-large BMLs were associated with M:L paBMD and M:L paBMD change. The MT BML volume change was classified into quartiles. We chose the middle two quartiles of BML volume change as the reference group. We used logistic regression models to evaluate the association between quartiles of changes in MT paBMD or M:L paBMD ratio, as outcomes, and change in MT BML volume (classified into three groups). The models were adjusted for age (<65 years, ≥ 65 years) and obesity (body mass index < 30 kg/m^2, ≥ 30 kg/m^2). Since only a small number of knees increased MT sclerosis scores we used Fisher Exact Tests to explore if the frequency of knees with sclerosis progression was different between BML volume change groups.

Results: The sample (n = 310), excluding those with LT BMLs, is described in the table. We found an association between greater MT paBMD change and BML regression (OR = 1.7 [95% CI = 1.1 - 2.8]) and a similar trend for BML progression (OR = 1.6 [95% CI = 1.0 - 2.6]). We also detected an association between increased M:L paBMD change and BML regression (OR = 1.6 [95% CI = 1.0 - 2.7]) or BML progression (OR = 1.8 [95% CI = 1.1 - 3.0]), although BML regression had borderline statistical significance. Exploratory analyses indicated that the frequency of sclerosis progression in the MT was greater among knees with BML progression or regression compared to knees with no BML change (p = 0.01 and p = 0.04; respectively).

Conclusions: Based on increased paBMD and sclerosis progression in the MT, knees with BML regression or BML progression were more likely to have peri-articular bone changes related to OA progression compared to knees with no BML change. BML regression on traditional MRI may not reflect an improvement in peri-articular bone quality.

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THE RELATION BETWEEN QUANTITATIVE DELAYED CONTRAST-ENHANCEMENT IN MENISCUS AND CARTILAGE IN KNEE OSTEOARTHRITIS

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Purpose: Quantitative analysis of delayed contrast-enhanced T1 values (T1GD) was proposed to give insight in meniscal damage and articular cartilage degeneration within one MR examination. However, unlike in delayed gadolinium-enhanced MRI of cartilage (dGEMRIC), contrast uptake in the meniscus is probably not determined by the glycosaminoglycan (sGAG) content and hence fixed charged density in the meniscus, but is rather based on the integrity of the collagen network. Despite the different factors which are believed to dominate contrast uptake in the meniscus and cartilage, it has been shown that there is a moderate relation of T1GD values of the meniscus and the adjacent cartilage in healthy volunteers and self-reported knee OA patients. This relation has, however, not yet been studied in patients diagnosed with OA. Therefore, the goal of this study was to explore the relation between

Table
Descriptive Characteristics of Knees with Medial Tibia Bone Marrow Lesion (BML) Regression, Progression, or No Change

Variable	BML Regression (n = 77) Median (Min, Max) or n (%)	No BML or No BML Change (n = 156) Median (Min, Max) or n (%)	BML Progression (n = 77) Median (Min, Max) or n (%)
Age (years)	65 (50, 81)	61 (48, 82)	68 (48, 82)
Body mass index (kg/m^2)	29.3 (21.1, 40.9)	29.4 (20.1, 42.0)	29.5 (19.6, 40.7)
Female	40 (52.0%)	85 (54.5%)	39 (50.7%)
Kellgren-Lawrence Grade ≥2	62 (80.5%)	95 (61.3%)	57 (74.0%)
BML Volume Change (cm^3)	-0.37 (-8.44, -0.14)	-0.02 (-0.13, 0.03)	0.21 (0.04, 6.77)
Medial Tibia paBMD (Change)	0.002 (-0.149, 0.164)	-0.011 (-0.107, 0.149)	-0.001 (-0.091, 0.168)
M:L paBMD Ratio (Change)	0.005 (-0.119, 0.291)	-0.007 (-0.102, 0.091)	0.003 (-0.080, 0.410)
Sclerosis Progression (Medial Tibia)	5 (6.9%)	2 (1.3%)	7 (10%)

Notes: paBMD: peri-articular bone mineral density, M:L paBMD Ratio: medial-to-lateral paBMD ratio.